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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/788,626	02/13/2001	Andrew J. Flint	200125.401	4380

500 7590 08/08/2002

SEED INTELLECTUAL PROPERTY LAW GROUP PLLC
701 FIFTH AVE
SUITE 6300
SEATTLE, WA 98104-7092

EXAMINER

PAK, YONG D

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 08/08/2002

13

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/788,626

Applicant(s)

FLINT ET AL.

Examiner

Yong Pak

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 June 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-32 is/are pending in the application.
- 4a) Of the above claim(s) 17-33 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-16 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7 and 8.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Claims 1-33 are pending.

Election/Restrictions

Applicant's election without traverse of Group I (claims 1-16) with an election of a human PTP-1B, wherein the tyrosine corresponding to amino acid position 46 of the PTP-1B amino acid sequence is replaced with a phenylalanine, in Paper No. 12 is acknowledged.

Claims 17-33 withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claim 14 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 12.

Claim Objections

Claims 9-10, 13 and 16 are objected for being drawn to non-elected species.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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Claims 1-13 and 15-16 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-13 and 15-16 are drawn to a genus of mutant PTP. Claims 1-4, 6-13 and 15-16 are drawn to a genus of substrates that bind to the mutant PTP.

The claims are directed to a genus of molecules described by function. The specification teaches the structure on only a few representative species of mutant PTP, the PTP1B mutant, C215S, D181A and D199A and substrates that bind to them. Thus, the scope of the claim includes numerous structural variants and the genera are highly variant because a significant number of structural differences between the genus members is permitted. Further, the specification fails to describe any other representative species by any identifying characteristic or properties other than the functionality of being a substrate-trapping mutant of a PTP or being a substrate to the PTP. The general knowledge and level of skill in the art do not supplement the omitted description because specific guidance is needed.

Given this lack of description of the representative species encompassed by the genus of the claims, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the inventions of claim 1-13 and 15-16.

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Claims 1-13 and 15-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of identifying agents that alter the interaction of a PTP1B-C215S, D181A or D199A and a labeled specific substrate, does not reasonably provide enablement for a method using any mutant PTP enzyme with any substrate. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Claims 1-13 and 15-16 are drawn to a method of use of a substrate-trapping mutant of any PTP. The specification does not teach mutant PTS other than the PTP1B-C215S, D181A or D199A. The art does not generally allow the prediction of changes in an arbitrary physical property based on changes in structure of an enzyme. While there are a great number of possible mutants, it is a priori unpredictable as to which mutant will exhibit the claimed properties. Therefore, the breadth of these claims is much larger than the scope enabled by the specification. Furthermore, while recombinant techniques are available, it is not routine in the art to screen large numbers

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of enzyme mutants and substrates where the expectation of obtaining similar activity is unpredictable based on the instant disclosure. Therefore, one of ordinary skill would require guidance, such as information regarding the specific amino acid changes which would result in a substrate-trapping mutant in order to use the methods of claims 1-13 and 15-16. Without such guidance, the experimentation left to those skilled in the art is undue.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1-7 are rejected under 35 U.S.C. 102(b) as being anticipated by Tonks et al.

Tonks et al. (WO 98/04712 – form PTO 1449) teach a method of identifying an agent, which alters the interaction between a substrate-trapping mutant of a protein tyrosine phosphatase (PTP) and a substrate capable of generating a fluorescence

energy signal (pages 6-7 and 16-17). Tonks et al. teach that to facilitate the determination of the presence of the protein/PTP complex, labeled phosphorylated substrates can be used, such as a fluorescein or a rhodamine and teaches that enzymatic activity assays are well known in the art, citing U.S. Patent No. 5,352,660 (page 13 and 16-17). Regarding claim 5, Tonks et al. teach several tyrosine phosphorylated peptides, such as p130^{cas}, EDG, p120 bcr:abl, MAP kinase, and insulin receptors (pages 14 and 15). Regarding claim 6, Tonks et al. teach a mutant PTP in which the invariant aspartate residue is replaced with an amino acid, which does not cause significant alteration of the K_{cat} to less than 1 per minute (page 14). Regarding claim 7, Tonks et al. also teach a substrate trapping mutant PTP comprising a PTP in which the wildtype protein PTP catalytic domain is mutated at an amino acid position occupied by a cysteine residue (page 3). Therefore, the teachings of Tonks et al. anticipates claims 1-7.

Claims 1-7 are rejected under 35 U.S.C. 102(e) as being anticipated by Tonks et al.

Tonks et al. (U.S. Patent No. 5,912,138 – form PTO 1449) teach a method of identifying an agent, which alters the interaction between a substrate-trapping mutant of a protein tyrosine phosphatase (PTP) and a substrate capable of generating a fluorescence energy signal (Column 3, line 45 through Column 4, line 9 and Column 9, lines 12-50). Tonks et al. teach that to facilitate the determination of the presence of the protein/PTP complex, labeled phosphorylated substrates can be used, such as a

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fluorescein or a rhodamine and teaches that enzymatic activity assays are well known in the art, citing U.S. Patent No. 5,352,660 (Column 7, lines 7-28 and Column 9, lines 12-50). Regarding claim 5, Tonks et al. teach several tyrosine phosphorylated peptides, such as p130^{cas}, EDG, p120 bcr:abl, MAP kinase, and insulin receptors (Column 7, lines 51-58). Regarding claim 6, Tonks et al. teach a mutant PTP in which the invariant aspartate residue is replaced with an amino acid which does not cause significant alteration of the K_{cat} to less than 1 per minute (Column 7, lines 29-42). Regarding claim 7, Tonks et al. also teach a substrate-trapping mutant PTP comprising a PTP in which the wildtype protein PTP catalytic domain is mutated at an amino acid position occupied by a cysteine residue (Column 2, lines 13-35). Therefore, the teachings of Tonks et al. anticipate claims 1-7.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 6 and 8-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tonks et al. in view of Jia et al.

Tonks et al. (WO 98/04712) teach a method of identifying an agent which alters the interaction between a substrate trapping mutant of a protein tyrosine phosphatase (PTP) and a substrate capable of generating a fluorescence energy signal, as discussed above. Tonks et al. also teach a substrate trapping PTPs where mutant or altered form of the PTP are used to bind or trap one or more substrate of the PTP, so that an enzyme-substrate complex can be readily observed (page 2). The mutant PTPs lacking catalytic activity or have reduced catalytic activity relative to the wild type PTP but retain the ability to bind tyrosine phosphorylated substrate (page 2).

The difference between the instant invention and the reference of Tonks et al. is that the reference of Tonks et al. does not teach a human PTP-IB wherein Tyr-46 is substituted with a phenylalanine residue.

Jia et al. (form PTO 1449) teach that Tyr corresponding to position 46 of PTP1B is one of a few residues, which are invariant within the PTP family and forms interactions with the main-chain atoms, and the aromatic ring of the substrate of PTP (page 1755). Jia et al. also teach that in a bacterial PTP, Phe is present instead of Tyr-46, suggesting that the mechanism of PTP substrate recognition maybe conserved.

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Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to use the method of Tonks et al. with a PTP-1B wherein one of the residues of the recognition site, Tyr-46, is mutated with a conservative substitution, a Phe residue. The motivation of using such a mutant PTP1B is to trap the substrate as described by Tonks et al. to readily observed the complex formed in the presence of an agent that alters the interaction between the PTP and the substrate. One of ordinary skill in the art would have had a reasonable expectation of success since residues in the recognition site or the signature motif have been mutated successfully and wherein the substrate is trapped by the PTP1B.

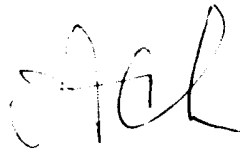
No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 703-308-9363. The examiner can normally be reached on 8:00 A.M. to 4:30 P.M weekdays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Yong Pak
Patent Examiner



August 5, 2002